line 2, after "sequence" insert --of-- and delete "substantially corresponding to".

IN THE ABSTRACT

Line 5, after "effects.", insert the following:

--Isolated DNA encoding TNF Binding Protein II is obtained and may be used to produce expression vectors, prokaryotic or eukaryotic expression hosts and methods of obtaining the protein by culturing of such hosts.--

Delete lines 6-11 (paragraphs 2 and 3).

REMARKS

Claims 11-14 and 34-45 presently appear in this case. Claims 14, 39, 42 and 45 have been withdrawn from consideration. No claims have been allowed. The Official Action of December 9, 1996, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to isolated DNA molecules which encode TBP-II. TBP-II is a novel tumor necrosis factor binding protein which is an extracellular domain of a TNF receptor. It was first disclosed in the parent applications of the parent application, and one claim directed to this protein was officially found to be allowable by the examiner in charge of the present case. The claims drawn to the protein in parent application of 07/930,443 are now involved in an interference proceeding with the claims of USP 5,344,915. The present

application claims any isolated DNA molecule encoding the novel TBP-II protein, as well as replicable expression vehicles capable of expressing that protein, host cells transformed with such replicable expression vehicles and processes for producing the protein by culturing such host cells.

The examiner has considered applicants' traversal of the restriction requirement but has deemed the requirement proper and, therefore, made it final. This action of the examiner is again respectfully traversed.

In the examiner's comments concerning applicants' traversal of the restriction requirement, the examiner stated, with respect to applicants' reference to MPEP §821.04, that no allowable claims are present in the instant application. This comment by the examiner does not respond to applicants' traverse. Whether or not the examiner presently considers the claims presented in this case to be allowable is irrelevant to the issue of whether or not the process claims will be rejoined with the product claims <u>if and when</u> such product claims are found to be allowable. If the examiner agrees that MPEP §821.04 is applicable to the present situation and that, if the product claims are eventually found to be allowable, the process claims will be rejoined, then applicants will be satisfied, and no petition to the Commissioner with respect to this restriction requirement will be necessary. On the other hand, if the examiner for some reason considers that the process claims will not be rejoined with the product claims regardless of the allowability of the product claims, then applicants will take an

immediate petition. It should be noted that, while the present application contains no allowable claims, none of the claims are subject to a prior art rejection.

Accordingly, all of the grounds for traversal presented in applicants' response of October 7, 1996, are preserved, and the examiner is requested to respond to applicants' query as to whether the non-elected claims will be rejoined with the elected claims if the elected claims are found to be allowable.

With respect to the examiner's comments about applicants' statement at page 4 of its response of October 7, 1996, relating to parent application 07/930,443, applicants' comments in this regard were not intended to be part of the response to the restriction requirement but were intended to be in the nature of an information disclosure statement, advising the examiner of the existence of the interference and patent 5,344,915. The examiner's statement that there are no allowed claims in application 07/930,443 is not exactly accurate. An application cannot be sent to interference unless there is at least one claim that is considered to be allowable, subject to the priority determination of the interference. One claim of the parent application has been considered to fully satisfy 35 USC §112, 35 USC §102 and 35 USC §103 so as to patentably define the novel protein TBP-II.

The examiner states that the drawings are informal for the reasons set forth in the enclosed form PTO-948. The examiner then repeats statements on the form 948 relating to

photographs. Of course, the examiner's comments about color photographs are totally irrelevant to the present application which contains no such color photographs. In any event, the rear of the form PTO-948 explicitly states that applicants may delay filing new drawings until receipt of the Notice of Allowability. Accordingly, the correction of the informalities, including the filing of an appropriate petition with black-and-white photographs, will be filed in due course.

The examiner states that the use of the trademarks AFFIGEL-10, AQUAPORE, SYNCHROPAK, MONO-Q and TWEEN 20 have been noted in this application. The examiner states that they should be capitalized wherever they appear and be accompanied by the generic terminology in order to respect the proprietary nature of these marks.

The proprietary nature of these marks has been respected in the present specification in view of the fact that each time they are mentioned, they are typed with initial capitalization and followed by the generic terminology, such as "Mono-Q and Mono-S columns". The generic terminology is "columns". In order to fully comply with the July 1996 revision of MPEP §608.01(v), each mention of these trademarks has now been amended to appear in all capital letters rather than merely initial capitalization. Accordingly, this requirement has now been overcome.

The examiner states that the Abstract of the Disclosure is objected to because it does not disclose the claimed invention and that correction is required.

The rules and the MPEP do not provide that an abstract must disclose the claimed invention but only that it be an abstract of the disclosure of the application. Nevertheless, the Abstract has now been amended to refer to the presently claimed invention, thus obviating this requirement. Furthermore, the title has now been amended in order to refer more directly to the presently claimed invention.

Claims 11 and 33-36 have been rejected under 35 USC §101 because the claims encompass products of nature and are, thus, not directed to patentable subject matter. The examiner states that applicants can overcome this rejection by amending the claims to read on an isolated or purified DNA.

The claims have now been amended to refer to an isolated DNA, thus obviating this rejection.

Claims 11-13, 13-38, 40, 41, 43 and 44 have been rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. The examiner states that there is no support in the specification for the recitation of "amino acid sequence substantially corresponding" in claim 11, and there is no support in the specification as originally filed for the DNAs of claims 35 and 36. This rejection is respectfully traversed.

Claim 11 has now been amended to delete the term "substantially corresponding", thus obviating this part of the rejection. The examiner has not explained why he considers that

claims 35 and 36 are not supported in the specification as originally filed. If the examiner is referring to a typographical error in the sequence, this has now been corrected, thus obviating the rejection. Otherwise, it is not understood why the examiner does not consider the claims to be supported by the written description. The N-terminal amino acid sequence is supported, for example, by the disclosure in the paragraphs bridging pages 23 and 24 of the present application. The least truncated sequence is disclosed at page 24, lines 7 and 8, and three different truncations are disclosed at page 23, lines 5 and 6 from the bottom, line 3 from the bottom and final line. This is simply claimed generically using the definitional term "Xaa" in the sequence. The ability of the protein to inhibit the cytotoxic effect of TNF-α on murine A9 cells is explicitly disclosed in the present specification in many places, such as at page 7, lines 3-4. The molecular weight of about 30 kDa when analyzed by SDS-PAGE under reducing conditions is disclosed, for example at page 7, lines 2-3. That the present inventors invented a DNA which encodes such protein is disclosed, for example, at page 8, lines 20-21, or claim 11 as originally filed. Accordingly, the written description requirement of the first paragraph of 35 USC §112 is fully complied with for each of claims 11, 35 and 36. If the examiner is to repeat this rejection, it is requested that the examiner explain in detail exactly what language is believed not to be supported by the written description of the specification.

Claims 11-13, 33-38, 40, 41, 43 and 44 have been rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable to one skilled in the art to which it pertains to make and/or use the invention. The examiner states that the specification does not adequately teach how to make the claimed nucleic acids as one cannot make that which one has no conception. The examiner states that the specification discloses a partial protein sequence and offers it up as enablement of nucleic acids encoding the isolated proteins. However, the examiner states that there is no disclosure of the complete sequence of any protein nor is there any disclosure of even a single nucleic acid that would meet the limitations of the claims. Thus, the examiner concludes that there is no teaching of structure that the artisan could use as a guide in making the claimed nucleic acids. The examiner states that in the absence of any working examples, any guidance as to the structure of the claimed nucleic acids and the unpredictability inherent in making nucleic acids to encode proteins which are defined almost solely by function, it would require undue experimentation to practice the claimed invention. The examiner relies on Amgen v. Chugai, 18 USPQ2d 1017 and Fiers v. Sugano 26 USPQ2d 1601, as well as In re Deuel, 34 USPQ2d 1210, for the conclusion that if an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has

occurred. The examiner states that it would require undue experimentation to produce the claimed DNA because there is no guidance in the specification as to what portion of the DNA molecule encodes the particular domain mediating the functional activity and that the claims encompass nucleic acids encoding innumerable muteins, variants and derivatives. The examiner states that in the absence of information as to the complete structure of the encoded proteins, as well as information as to the structure-function relationship of the proteins, it would require undue experimentation to practice the invention in a manner commensurate in scope with the claims. The examiner states that there is no disclosure in the specification as to whether the particular amino acid sequences listed on page 23 are derived from the same molecule or that the molecule is found as four different but related molecules or whether the four potential forms of TBP-II are functionally active or the nature of the identity of the functionally active molecule. The examiner states that one cannot claim nucleic acids via a single biological function. This rejection is respectfully traversed.

First of all, it must be made absolutely clear that applicants are not claiming DNA encoding any molecule having a given function. Applicants are claiming DNA encoding a single, novel protein first discovered by the present inventors. The examiner in the parent case has found that a protein claim of the scope in which the protein is claimed in claim 36 is fully enabled by the present specification and fully complies with the written description requirement, and this claim, as well as

others, have been forwarded to the Board of Patent Appeals and Interferences for the determination of a priority issue. Claim 11 has now been amended to delete reference to proteins having an amino acid sequence substantially corresponding to TBP-II. The DNA molecule of the present invention comprises the nucleotide sequence coding for a protein consisting of TBP-II with this single, novel protein being defined by a partial amino acid sequence, as well as by its properties.

With respect to the examiner's comment that there is no guidance in the specification as to whether the four potential forms of TBP-II are derived from the same molecule or that the molecule is found as four different but related molecules, the examiner's attention is invited to Section 1.5 at pages 23-24 of the present specification. The present specification clearly refers to TBP-II as a single molecule of which the N-terminal sequence may be truncated by up to five amino acids. It is only the examiner that is suggesting that four different but related molecules may exist. The specification does not teach this. The specification teaches that a single molecule has been found which molecule may have certain truncations at its N-terminus. Certainly, one of ordinary skill in the art would not consider that a truncation of up to five residues at the N-terminus of a 30 kD protein would affect the function of that protein, particularly when the function is simply binding to TNF. Respectfully, the examiner is embarking on hypothetical excursions which are not necessitated by the present specification. The present

specification teaches that TBP-II is a single molecule which may have four different truncations at its N-terminus. The statements to this effect were accepted at face value during the prosecution of the parent case, in which a claim to the TBP-II protein was found to be allowable, including its four possible N-terminal truncations. The same is true with respect to the prosecution of patent 5,344,915, which is in interference with the parent application. Statements in a specification must be accepted unless there are good and scientifically supported reasons why those of ordinary skill in the art would doubt such presumptively accurate statements (MPEP §2164.04). The examiner has not provided such support for doubting the statement in the present specification that a single TBP-II molecule has been described with various truncated forms, as opposed to four different but related molecules.

Further, Ex parte Maizell is inapplicable, as applicants are not claiming all molecules having a certain biological function. Applicants are claiming the single molecule TBP-II, which is defined not only by its function, but also by a partial amino acid sequence. This definition is sufficient to distinguish the protein encoded by the DNA of the present invention from all other existing proteins. As opposed to Maizell, the present claims do not try to cover all "biologically functional equivalents" of TBP-II. Thus, the Maizell case is inapplicable to the present fact situation.

Once it is accepted that the claims are directed to DNA comprising a nucleotide sequence encoding only a single

protein, albeit with four different defined possible truncations at its N-terminal sequence, then most of the examiner's comments in the rejection become moot.

As to the examiner's citation of the Amgen, Fiers and Deuel cases, these cases are distinguishable from the present fact situation. In each of those cases, applicants were attempting to claim a single DNA sequence, which is the natural sequence encoding a particular protein. Here, applicants are not attempting to claim a single, natural sequence. In the present fact situation, the protein is not a well-known protein which existed in the prior art, as was the case with erythropoietin and IFN beta of Amgen and Fiers, respectively. In the present case, the protein encoded by the DNA is a novel protein, and the DNA claims are intended to cover any sequence which encodes the novel protein. Once one knows the amino acid sequence of a novel protein, all of the DNA sequences encoding that protein are automatically known in view of the genetic code. If the entire amino acid sequence for the protein had been disclosed in the present specification, it is not believed that the examiner would have considered that there were any grounds for an enablement rejection of the DNA because every DNA which encodes that protein could be readily conceived by simply using the genetic code. Once conceived, such DNA sequences could be produced by those of ordinary skill in the art without undue experimentation. This has been explicitly confirmed as PTO policy in "Training Materials for Examining Patent Applications with Respect to 35 U.S.C. §112, First Paragraph--

Enablement Chemical/Biotechnical Applications". In Section III.A.2.b.i.(c), these training materials state:

> When claims are directed to any purified and isolated DNA sequence encoding a specifically named protein wherein the protein has a specifically identified sequence, a scope rejection is generally not appropriate.
>
> ...
>
> The Deuel claims 4 and 6 were directed to any DNA that would encode a specific amino acid sequence. Claims 4 and 6 recited only one amino acid sequence each, and each claim was directed to all nucleic acid sequences that encode the respective amino acid sequence. The various genetic codes are well known. Thus, to list all cDNA of the sequences that encode a given amino acid sequence simply requires reverse translating the amino acid sequence to the nucleic acid sequence. Theoretically, one armed only with a pencil, paper and the genetic code could list all of the cDNA that encode the two amino acid sequences mentioned in the claims. Admittedly, this could not be done in practice even by a fast computer because claim 4 embraces 2.09×10^{75} embodiments. However, any one of the embodiments could be readily determined. As to actually obtaining the cDNA, this could be done by simply writing down the sequence and ordering it from a company that custom synthesizes DNA.

Thus, it is clearly PTO policy to permit claims directed to any purified and isolated DNA sequence encoding a protein with a specifically identified sequence.

Here, the protein is not defined by its sequence, but is, indeed, adequately defined and fingerprinted by a partial amino acid sequence in combination with disclosure of certain biological properties. The fact that the protein of the present invention is adequately defined, is evidenced by the fact that

at least one claim was found to be allowable in the present case before forwarding the application to the Interference Branch for a determination of a priority dispute. It is further evidenced by the allowance of the claims in patent 5,344,915, which also claimed the protein only by a partial amino acid sequence and biological properties. Once the protein has been defined sufficiently to fingerprint it, including reference to a partial amino acid sequence, the entire amino acid sequence of that protein is inherent in the otherwise adequately defined protein molecule. As the full sequence of this protein is inherent and determinable by those of ordinary skill in the art reading the present specification without undue experimentation, the present application should be considered in the same manner as an application which explicitly discloses the entire sequence.

Accordingly, as the entire sequence of the single protein molecule of the present invention is inherent and readily determinable by those of ordinary skill in the art reading the present specification without undue experimentation, a claim encompassing all DNA within the genetic code which encodes that sequence is fully conceived and enabled for the same reason that the protein is fully conceived and enabled. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

Claims 11-13, 33-38, 40, 41, 43 and 44 have been rejected under 35 USC §112, second paragraph, as being indefinite. The examiner states that claim 11 is indefinite in the recitation of "substantially corresponding" because it is

unclear what this means or encompasses in the context recited in the claim, and claims 33 and 34 have been rejected as indefinite in the recitation of "in accordance" because it is unclear what this means or encompasses in the context recited in the claims. This rejection is partially traversed.

Claim 11 has now been amended in order to delete recitation of "substantially corresponding". Accordingly, this rejection has now been obviated for claim 11 and all those claims dependent therefrom. It is not understood why the examiner has included claims 35 and 36 in this rejection as these claims do not contain any of the language to which the examiner has objected.

With respect to the language "in accordance", as appearing claims 33 and 34, applicants' attorney considers this rejection rather strange as this is simply standard claim terminology for dependent claims. "A _____ in accordance with claim _____" or "The _____ according to claim _____" or "The _____ of claim _____" are all merely alternative claim-drafting techniques commonly used for reciting any dependent claim. In over twenty-five years of patent prosecution, undersigned has used this language in nearly every application which he has written and has never had it objected to by an examiner. The examiner is invited to take any ten patents at random out of a search shoe, and it is believed that the examiner will find this language used is one or more of them. Claims 33 and 34 are dependent claims and, thus, are subject to the requirements of 35 USC §112, fourth paragraph. Claims 33 and 34 satisfy this

paragraph in that they contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. The language "in accordance with" is merely a commonly used claim-drafting technique to refer back to a claim previously set forth. Clearly, the remainder of these claims incorporates by reference all of the limitation of the claim to which it refers and then specifies a further limitation of the subject matter claimed. This fully complies with all paragraphs of 35 USC §112. Reconsideration and withdrawal of this part of the rejection is respectfully urged.

Please take note that the present application has included claims which correspond substantially to the claims of U.S. Patent 5,395,760 since a date prior to one year from the date on which the patent was granted (see 35 USC §135(b). This notification is also intended to satisfy 37 CFR §1.607(c).

It is submitted that all of the claims now present in the case clearly define over the references of record. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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